

# Welcome to today's FDA/CDRH Webinar

Thank you for your patience while we register all of today's participants.

If you have not connected to the audio portion of the webinar, please do so now:

Dial: 888-945-5897

International Callers: 1-517-308-9291

Passcode: 8862552

# FDA's Proposed Framework for Regulatory Oversight of Laboratory Developed Tests (LDTs)

Katherine Serrano

Deputy Director, Division of Chemistry and Toxicology Devices

Office of In Vitro Diagnostics and Radiological Health

Center for Devices and Radiological Health



### **Purpose and Scope of Webinar**

- To provide an overview and context of the proposed oversight framework
- To answer clarifying questions about the specific proposals in the draft guidances
- Goal: enable stakeholders to provide better feedback to the dockets



#### **Overview**

- Background
  - IVD regulation
  - Need for greater oversight of LDTs
- Initial public feedback in 2010
  - Oversight framework suggestions
- FDA's current proposal
  - Continued enforcement discretion in some areas
  - Timeframe for enforcement in other areas
- Next Steps
  - Discussion of FDA's current proposal



### **IVD** Regulation

- Through the 1976 Medical Device Amendments to the FFDCA, FDA has the authority to regulate all in vitro diagnostics (IVDs) as devices, including laboratory tests, regardless of whether they are developed and manufactured by a laboratory or a conventional device manufacturer.
- FDA has generally exercised enforcement discretion (i.e., generally not enforced applicable provisions under the FFDCA and FDA regulations) for Laboratory Developed Tests (LDTs), which FDA defines as:

an IVD that is intended for clinical use and designed, manufactured and used within a single laboratory.



# Public Health Need for Greater Oversight

- Evolution of LDT technology, marketing, and business models has:
  - Increased risk associated with LDTs
  - Created gaps in LDT Oversight
- Consequences
  - Significant adverse health consequences
  - Unnecessary healthcare costs
  - Could undermine progress of personalized medicine, which depends on tests that work



# Public Health Need for Greater Oversight

FDA identified as the Agency to provide needed oversight by:

- National Human Genome Research Institute (Department of Energy & National Institutes of Health; 1997)
- Secretary's Advisory Committee on Genetic Testing (2000)
- Secretary's Advisory Committee on Genetics, Health, and Society (2008)
- Institute of Medicine (2012)



# **Initial Public Feedback (2010)**

FDA held a public meeting *PRIOR* to developing the proposed regulatory oversight framework





# **Initial Public Feedback (2010)**

- Oversight Framework Suggestions
  - Process should allow for stakeholder input and leverage external experts
  - Should use risk-based, phased-in strategy
  - Should provide reasonable transition period
  - Should provide clear definition of LDTs
  - Registry of all tests
    - Partnerships with other agencies
  - Process to address emerging diseases/emergency situations



# **Initial Public Feedback (2010)**

- Oversight Framework Suggestions (continued)
  - Less oversight for certain categories of tests
    - Rare Diseases
    - No FDA approved/cleared alternative
    - Hospital based tests
    - Tests with extensive peer review
    - Tests performed in accredited lab or already approved by NY state
  - Post-Market Surveillance needed to protect public health
  - Significant Education/Outreach needed

# FDA's Current Proposal

- 1. Enforce R&L with option for notification (no-fee alternative to R&L) to collect basic information on LDTs
- 2. Enforce Adverse Event Reporting
- 3. Use public process (including advisory panel) to obtain input on risk and priority for oversight
- 4. Phase-in enforcement of premarket review and QS requirements over ~9 years based on risk
- 5. Continue some enforcement discretion for specific categories.

#### "Traditional" LDTs

#### Proposed oversight:

- Enforcement discretion for premarket review and QS
- Enforcement of R&L (with option for notification) and MDR

#### Proposed factors for enforcement discretion:

- Whether it is an LDT (designed, manufactured and used within a single lab);
- Whether it is manufactured and used by a health care facility lab (such as one located in a hospital or clinic) for a patient that is being diagnosed and/or treated at that same health care facility or within the facility's healthcare system;
- Whether it is comprised only of components and instruments that are legally marketed for clinical use; and
- Whether it is interpreted by qualified laboratory professionals without the use of automated instrumentation or software for interpretation.

#### **LDTs for Rare Diseases**

#### Proposed oversight:

- Enforcement discretion for premarket review and QS
- Enforcement of R&L (with option for notification) and MDR

#### Proposed factors for enforcement discretion:

- Whether it is an LDT (designed, manufactured and used within a single lab); and
- Whether it meets the definition of a Humanitarian Use Device (HUD) under 21 CFR 814.102(a)(5) (i.e., number of persons who may be tested is fewer than 4,000 per year in the United States)

#### **LDTs for Unmet Needs**

#### Proposed oversight:

- Enforcement discretion for premarket review and QS
- Enforcement of R&L (with option for notification) and MDR

#### Proposed factors for enforcement discretion:

- Whether it is an LDT (designed, manufactured and used within a single lab);
- Whether there is no cleared or approved IVD available for the specific intended use; and
- Whether it is manufactured and used by a health care facility lab (such as one located in a hospital or clinic) for a patient that is being diagnosed and/or treated at that same health care facility or within the facility's healthcare system.

### **Oversight Framework Proposal**

	Notifi- cation*	MDRs	Premarket Review	QS Reg.	R&L **
LDTs used solely for <b>forensic</b> purposes					
LDTs used in CLIA-certified, high-complexity histocompatibility labs for <b>transplantation</b>					
Low-risk (Class I) LDTs	٧	٧			
LDTs used for rare diseases per HUD definition	٧	٧			
"Traditional" LDTs	٧	٧			
LDTs for <b>unmet needs</b> when no FDA cleared/approved alternative exists	٧	٧			

<sup>\*</sup> Notification is not a requirement but an option to R&L.

<sup>\*\*</sup>FDA intends to continue exercising enforcement discretion for R&L provided notification is completed.

# Proposed Phase-In (based on final guidance publication)

	Notifi- cation*	MDRs	Premarket Review	QS Reg.	R&L
<ul> <li>Highest risk LDTs already on market</li> <li>LDTs with same intended use as cleared/approved companion diagnostics</li> <li>LDTs with same intended use as approved Class III medical devices</li> <li>Certain LDTs for determining safety or effectiveness of blood or blood products</li> </ul>	6m	6m	1y	Upon PMA submi ssion	Upon PMA approv al
Subsequent high risk LDTs in priority order developed with input through public process	6m	6m	2-5y	Upon PMA submi ssion	Upon PMA approv al
Moderate risk LDTs in priority order developed with input through public process	6m	6m	5-9y	Upon 510k cleara nce	Upon 510k cleara nce

<sup>\*</sup> Notification is not a requirement but an option to R&L.



- Premarket review for all NEW (i.e., not currently marketed) LDTs that:
  - Have the same intended use as cleared/approved companion diagnostics
  - Have the same intended use as approved Class III medical devices
  - Certain LDTs for determining safety or effectiveness of blood or blood products



- By 6m: Notification (or R&L) and adverse event reporting for all currently marketed LDTs except:
  - those used solely for forensic purposes
  - those used in CLIA-certified, high-complexity histocompatibility labs for transplantation
- After 6m: Notification (or R&L) of all NEW LDTs prior to marketing
  - includes notification for significant changes to the marketed intended use of existing LDTs



- Premarket submission for currently marketed LDTs that:
  - Have the same intended use as cleared/approved companion diagnostics
  - Have the same intended use as approved Class III medical devices
  - Certain LDTs for determining safety or effectiveness of blood or blood products
- Compliance with QS reg at time of PMA submission
- Compliance with R&L upon PMA approval



- Public process to get input on classification for existing LDTs
  - Will include use of advisory panel
  - Will issue draft guidance on LDT device classification for public comment
- Public process to get input on priority for remaining high-risk LDTs
  - Will include use of advisory panel



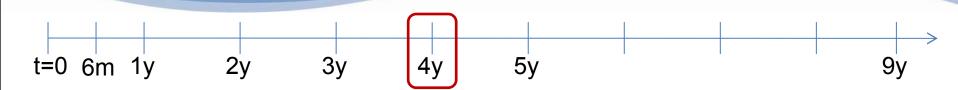
- Publication of a guidance on LDT device classification
- Publication of priority list for remaining high-risk LDTs



- Premarket submission for first prioritized high-risk group
  - Compliance with QS reg at time of PMA submission
  - Compliance with R&L upon PMA approval



- Premarket submission for all remaining high-risk
   LDTs according to priority list announced at year 2
  - Compliance with QS reg at time of PMA submission
  - Compliance with R&L upon PMA approval
- Public process to get input on priority for remaining moderate-risk LDTs
  - Will include use of advisory panel

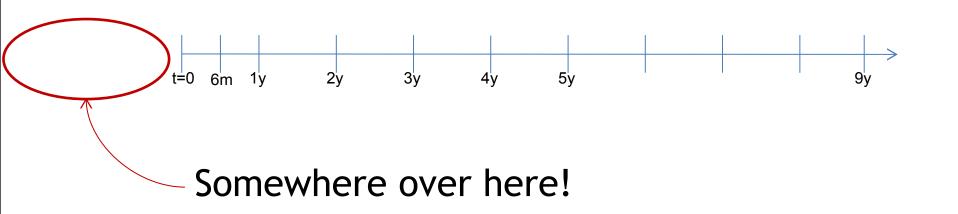


- Publication of priority list for moderate-risk LDTs
  - After considering input received through public process including advisory panel



- Premarket submission for all moderate-risk LDTs according to priority list announced at year 4
  - FDA anticipates use of third party reviewers
  - Compliance with QS reg at time of 510(k) clearance
  - Compliance with R&L at time of 510(k) clearance

# Where are we today?



FDA does not intend to implement the proposed enforcement policy for LDTs prior to publication of final guidances.

#### What's Next

- Public discussion of draft oversight framework
  - 120 day public comment period
  - Public Workshop in January

Goal: to work with all stakeholders to determine a framework for oversight that is in the best interest of public health

- FDA analysis of public input and incorporation of appropriate revisions in the final guidances
- Publication of final guidances (t=0 in timeline)
- Implementation

### What's on the table for discussion?

# Everything in the draft guidances



DEPARTMENT OF HEALTH AND **HUMAN SERVICES** 

Food and Drug Administration

[Docket No. FDA-2011-D-0360]

Framework for Regulatory Oversight of Laboratory Developed Tests; Draft Guidance for Industry, Food and Drug Administration Staff, and Clinical Laboratories; Availability

AGENCY: Food and Drug Administration

HHS.

ACTION: Notice.

www.federalregister.gov SUMMARY: The Admini .sight of Laboratory Developed Tests (LDTs)." This document describes a risk-based framework for addressing the regulatory oversight of a subset of in vitro diagnostic devices (IVDs) referred to as laboratory developed tests (LDTs), which are intended for clinical use and designed, manufactured and used within a single laboratory. This document describes FDA's priorities for enforcing pre- and post-market requirements for LDTs, and the process

#### "Traditional" LDTs

- Proposed oversight:
  - Enforcement discretion for premarket
- Do risk mitigations support enforcement discretion for R&L and MDRs?
- Enforcement of R&L (with option for notification) and MDR
- Proposed factors for enforcement discretion:
  - Whether it is an LDT (designed, manufactured and used within a single lab);
  - Whether it is manufactured and used by a health care facility lab (such as one located in a hospital or clinic) for a patient that is being diagnosed and/or treated at that same health care facility or within the facility's healthcare system;
  - Whether it is comprised only of components and instead legally marketed for clinical use; and
  - Whether it is interpreted by qualified laboratory processionals without the use of automated instrumentation or software for interpretation.

Are the other risk mitigations sufficient?

#### **LDTs for Rare Diseases**

- Proposed oversight:
  - Enforcement discretion for premarket review and QS
  - Enforcement of R&L (with option for notification) and MDR

Are these factors appropriate? If not, what?

- Proposed factors for enforcement discretion:
  - Whether it is an LDT (designed, manufactured and used within a single lab);
     and
  - Whether it meets the definition of a Humanitarian Use Device (HUD) under 21 CFR 814.102 (a)(5) (i.e., number of persons who may be tested is fewer than 4,000 per year in the United States)

#### **LDTs for Unmet Needs**

- Proposed oversight:
  - Enforcement discretion for premarket review and
  - Enforcement of R&L (with option for notification) a

Are the other risk mitigations sufficient?
If not, how should healthcare system be described?

- Proposed factors for enforcement discretion:
  - Whether it is an LDT (designed, manufactured and used within a single lab);
  - Whether there is no cleared or approved IVD available for the specific intended use; and
  - Whether it is manufactured and used by a health care facility lab (such as one located in a hospital or clinic) for a patient that is being diagnosed and/or treated at that same health care facility or within the facility's healthcare system

# What else should be clarified in the guidances?

What else should be addressed or further clarified in the guidances?

- How to interpret what elements make up a medical device
- What might constitute the label or labeling for a device
- Whether UDI requirements apply to LDTs
- How laboratory-physician communication about a test and its result would be viewed by FDA

#### **Comment Process**

	Framework draft guidance Pocket No. FDA-2011-D-0360	Notification/MDR draft guidance Docket No. FDA-2011-D-0357	
1. Electronic comments	http://www.regulations.gov/#!submit Comment;D=FDA-2011-D-0360-0002	http://www.regulations.gov/#!submit Comment;D=FDA-2011-D-0357-0002	
2. Written (must include docket No.)	Division of Dockets Management (HFA-305)  Food and Drug Administration  5630 Fishers Lane, rm. 1061  Rockville, MD 20852		
3. Public meeting	TBD early January 2015 Will be announced at <a href="http://www.fda.gov/LDTs">http://www.fda.gov/LDTs</a>		



### **Questions?**

LDTframework@fda.hhs.gov

Slide Presentation, Transcript and Webinar Recording will be available at:

www.fda.gov/CDRHWebinar under the "Past Webinars and Stakeholder Calls-2014" tab.